(b) obtaining a set of single-stranded oligomers E_i and $\underline{E}_i$ representing the components of a vector **V**, wherein the concentrations of said oligomers E_i and $\underline{E}_i$ are proportional to the absolute values of the amplitudes V_i of the vector components they represent,

wherein oligomers that represent components of said matrix **T** and said vector **V** having different basis vectors do not hybridize under conditions in which complementary oligomers E_i and $\underline{E}_i$ corresponding to the same basis vector $\boldsymbol{e}_i$ do hybridize;

(c) obtaining a set *S* of single-stranded oligomers E_i and $\underline{E}_i$ having the sequences of the A portions of those dimeric oligomers representing matrix T_{ij} which also comprise in their B portions sequences which are either the same as or complementary to the oligomers representing said vector **V**,

wherein the set of single-stranded oligomers ***S*** is an analog representation of the inner product of said matrix **T** and said vector **V**.

REMARKS

Regarding the Requirement to Identify SEQ ID NOS of Sequences in the Specification

Amendment of the specification to identify the SEQ ID NOS of the nucleic acid sequences disclosed on pages 26 and 32 was requested on page two of the Preliminary Amendment that was filed with the Sequence Listing on July 12, 1999. A copy of the Preliminary Amendment is attached.

Amendment of the Specification

The abstract is amended to be 250 words or less, as requested in the Official Action. A replacement sheet for page 68 of the specification with the amended abstract is attached to this amendment.

Amendment of the Claims

Claim 11 is amended by limiting section (i) to recite "phosphorylating or de-phosphorylating a terminus of an oligomer in an enzyme-catalyzed reaction." Support for this amendment is found in the specification at page 33, line 23, to page 34, line 4, which teaches removal of phosphate groups from termini of oligomers with a phosphatase enzyme, and addition of phosphate groups to termini of oligomers with a polynucleotide kinase enzyme.

Claims 17, 25, and 26 are amended to recite that memory matrix T_{ij} is the sum of all of the outer products $V_i^a V_i^a$ for $i \neq j$, as described on page 48, lines 6-8, of the specification.

Section (c) of claim 17 is also amended to more clearly identify what is meant by the recited set of oligomers comprising a "complete, sub-stoichiometric set of E_i and $\underline{E}_i$." Support for this amendment is found in the specification at page 49, line 12-21; and page 50, lines 17-20.

Claim 17 is further amended by adding to section (d) the limitation that steps (b) and (c) are repeated iteratively "until successive iterations yield the same" set of oligomer strands x_i that represents data set V_i^b. Support for this amendment is found in the specification at page 47, lines 4-9, and page 48, lines 2-5.

Claim 22 is amended to recite that the oligomers <u>of step (c)</u> are anchored to a support; as described, for example, at page 49, lines 12-14, line of the specification.

Claim 27 is amended by changing the labels $V_{\underline{i}}$, W_i, and $\underline{W_i}$ referring to the recited vectors to $\boldsymbol{V}$, $\boldsymbol{W}$, and $\underline{\boldsymbol{W}}$, respectively. This change is one of form only - it is requested so that the claim uses the same vector labels as are used in pages 31-33 of the specification to describe an oligomer-based method for representing obtaining the inner product of two vectors.

Claims 27 and 28 are also amended to recite that the oligomers that represent components of the recited vectors and/or matrix having different basis vectors do not hybridize under

conditions in which complementary oligomers E_i and $\underline{E_i}$ corresponding to the same basis vector $\boldsymbol{e}_i$ do hybridize. Support for this amendment is found, for example, at page 27, lines 5-14, and page 28, lines 10-12.

Claim 15 is amended by inserting a space immediately before the "2" in "i = 1,2, ..." in each occurrence of this term (correction of an informality).

The Applicants submit that the claims amended as described above do not contain new matter.

<u>Rejection of claims 11, 17, 25, and 26 under 35 U.S.C. 112, 1st paragraph, for containing new matter:</u>

A. <u>Regarding the rejection of claim 11:</u>

Section (g) of claim 11 is described in the Office Action as containing new matter because the specification does not provide support for generic addition of oligomer subunits to the end of an oligomer in an enzyme-catalyzed reaction as recited in item (g), but only supports such addition by a ligase-catalyzed reaction. The Applicants submit that in addition to teaching ligase-mediated addition, the specification describes adding oligomer subunits to the end of an oligomer using terminal transferase (see p. 31, line 23, to page 32, line 1) and by template-directed polymerase extension (see p. 38, lines 15-23). At the time the invention was made, one skilled in the art would also have known of other common methods for adding nucleotides to the end of an oligomer in an enzyme-catalyzed reaction; for example, by using T4 Ligase to add a nucleotide to the 3' end of a single stranded DNA or RNA (see BioLabs 1994 catalog, p. 70).

Section (i) of claim 11 is amended to recite phosphorylating or de-phosphorylating a terminus of an oligomer in an enzyme-catalyzed reaction. As noted above, the specification

discloses adding a phosphoryl group to a terminus of an oligomer with a polynucleotide kinase enzyme, and removing a phosphoryl group from a terminus of an oligomer with a phosphatase enzyme (see page 33, line 23, to page 34, line 4). At the time the invention was made, one skilled in the art would also have known of other common methods for modifying the state of phosphorylation of an oligomer terminus in an enzyme-catalyzed reaction; for example, by using T4 Polynucleotide Kinase or Calf Intestinal Alkaline Phosphatase to remove a 3' phosphoryl group from an oligomer prior to ligation or polymerase extension (see BioLabs 1994 catalog, pages 74-75).

The Applicants respectfully submit that sections (i) and (g) of claim 11 do not contain new matter, and that claim 11 as amended fully complies with the written description requirement. The Applicants observe that, according to the Revised Interim Guidelines for examination of compliance with the written description requirement published December 21, 1999, the essential objectives of the written description requirement are "to clearly convey the information that an applicant has invented the subject matter which is claimed," and "to put the public in possession of what the applicant claims as the invention;" and that the "fundamental factual inquiry" to be made in determining whether the subject matter of an amended claim complies with the written description requirement is "whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." The Federal Register, Volume 64, Number 244, Notices: Pages 71427-71440, December 21, 1999, see page 71434. Section II (3) (a) of the Revised Interim Guidelines states that in determining whether there is sufficient written description to inform a skilled artisan that Applicant was in possession of the claimed Invention as a whole at the time the application was filed, "[t]he description need only describe in detail

that which is new or not conventional," that "[w]hat is conventional or well known to one skilled in the art need not be disclosed in detail;" and that "[i]f a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met." (see page 71435). Section II (3) (b) of the Revised Interim Guidelines further states that "[t]o comply with the written description requirement of 35 U.S.C. 112, para. 1 ... each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure." (see page 71435).

The Applicants submit that the claimed invention as a whole relates to making and using oligomers that represent m-component vectors and vector and matrix operations in which said vectors participate, including vector and matrix operations that implement an analog neural network, and that section (g) and amended section (i) of claim 11 recite well-known methods for modifying oligomers that are described and exemplified in the specification with respect to practicing the disclosed invention. Given that the specification teaches that the enzyme-catalyzed reactions recited in sections (g) and (i) of claim 11 are useful in practicing the claimed invention, and provides several examples of how one skilled in the art could carry out the recited reactions, as discussed above; and given that at the time the application was filed, one skilled in the art would also have known of other ways of executing the recited procedures, in addition to those disclosed in the specification, the Applicants submit that the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date, they were in possession of the invention as recited in items (g) and (i) of claim 11.

B. Regarding the rejection of claims 17, 25, and 26 for containing new matter:

Section (d) of claim 17 is amended to recite that steps (b) and (c) are repeated iteratively until successive iterations yield the same data set representing V_i^b. The Applicants submit that amended claim 17 recites the element of convergence to a data set representing V_i^b as called for in the paragraph bridging pages 3-4 of the Office Action, and is in compliance with the written description requirement.

Claims 17, 25, and 26 are described in the Office Action as containing new matter because the claims recite memory matrix T_{ij} but do not specify that T_{ij} is the sum of all of the outer products $V_i^a V_j^a$ as disclosed on p. 48, lines 6-11, of the specification. Claims 17, 25, and 26 are amended to recite that memory matrix T_{ij} is the sum of all of the outer products $V_i^a V_i^a$ for $i \neq j$, as called for in the paragraph at the bottom of page 4 of the Office Action. The Applicants submit that amended claims 17, 25, and 26 comply with the written description requirement.

Given that a skilled artisan would have known how to practice the method of item (g) of claim 11 using any of several molecular biological techniques described in the specification or in common use at the time of filing, and in view of the amendment of item (g) of claim 11, and of claims 17, 25, and 26 in response to the Office Action, as discussed above, the Applicants respectfully submit that the claims do not contain new matter, and that the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the art that at the time of filing, the inventors had possession of the claimed invention. Accordingly, the Applicants respectfully request that rejection of the claims under 35 USC 112, 1st paragraph, for containing new matter, be withdrawn.

Rejection of claims 13, 15, 27, and 28 under 35 U.S.C. 112, 1st paragraph, for encompassing more than is supported by the specification

A. Regarding the rejection of claim 13 for unsupported scope:

The Office Action states that claim 13 is only enabled for addition where the vectors are exactly oppositely oriented in vector space.

The Applicants submit that the method recited in claim 13 is fully supported by the specification, even for addition of vectors that are not oppositely oriented. As described on pages 5 and 26-27 of the specification, a vector $\boldsymbol{V}$ of the form $\boldsymbol{V} = V_1\, \boldsymbol{e}_1 + V_2\, \boldsymbol{e}_2 \ldots + V^a{}_m\, \boldsymbol{e}_m$ is represented in the claimed invention by a set of 2m different oligomers which represent basis vectors $\boldsymbol{e}_i$ for i = 1 to m. The number of different oligomers is 2m, because each basis vector $\boldsymbol{e}_i$ can be represented by one of two complementary oligomers E_i or $\underline{E}_i$, depending on whether the sign is positive or negative, respectively. As described in the specification (p. 5, lines 13-15), and as recited in claim 9, the concentration of each of the oligomers E_i or $\underline{E}_i$ is proportional to the absolute value of the amplitude V_i of the i-th component of $\boldsymbol{V}$. If the ith component, $V_i\boldsymbol{e}_i$, of a vector of the present invention is positive, it is represented by a set of oligomers E_i , the concentration of which is proportional to the amplitude V_i. If the value of $V_i\boldsymbol{e}_i$ is zero, the set of oligomers representing the vector is empty; i.e., it contains no oligomers corresponding to basis vector $\boldsymbol{e}_i$. Likewise, a negative value of $V_i\boldsymbol{e}_i$ is represented by a set of oligomers $\underline{E}_i$, the concentration of which is also proportional to the absolute value of amplitude V_i. As described in the specification, addition of two vectors $\boldsymbol{V}^a$ and $\boldsymbol{V}^b$ is represented by the set of single-stranded oligomers that remains after pooling the oligomers that represent the two vectors, even if none, or only some, of the oligomers that represent $\boldsymbol{V}^a$ are complementary to oligomers that represent $\boldsymbol{V}^b$. For example, let vector $\boldsymbol{V}^a$ be defined as:

$$\boldsymbol{V^a} = V^a_1\, e_1 + V^a_2\, e_2 + V^a_3\, e_3 + V^a_4\, e_4 + V^a_5\, e_5 + V^a_6\, e_6 + V^a_7\, e_7 + V^a_8\, e_8,$$

let vector $\boldsymbol{V^b}$ be defined as

$$\boldsymbol{V^b} = V^b_1\, e_1 + V^b_2\, e_2 + V^b_3\, e_3 + V^b_4\, e_4 + V^b_5\, e_5 + V^b_6\, e_6 + V^b_7\, e_7 + V^b_8\, e_8,$$

let vector amplitudes V^a_1 to V^a_4 and V^a_6 of $\boldsymbol{V^a}$, and V^b_1 to V^b_5 of $\boldsymbol{V^b}$ all equal zero,

let vector amplitudes V^a_5, V^a_7 and V^a_8 of $\boldsymbol{V^a}$, and V^b_6 and V^b_7 of $\boldsymbol{V^b}$ all have positive values (>0),

and let vector amplitude V^b_8 of $\boldsymbol{V^b}$ have a negative value; then:

$$\boldsymbol{V^a} + \boldsymbol{V^b} = (V^a_1 + V^b_1)\, e_1 + (V^a_2 + V^b_2\, e_2) + \ldots (V^a_8 + V^b_8\, e_8).$$

(see also, Riddle, Calculus and Analytic Geometry, 2nd Edition, Wadsworth Publishing Co., Belmont, Ca, 1974, page 622).

In representing this example of vector addition by the method of the present invention, the set of single-stranded oligomers representing the sum of vectors $\boldsymbol{V^a}$ and $\boldsymbol{V^b}$ (the "answer set") would be as follows:

(a) the answer set would contain no oligomers corresponding to basis vectors e_1 to e_4 because the value of these components was zero in both vectors;

(b) the oligomers in the answer set corresponding to basis vector e_5 would consist solely of the oligomers contributed by component $V^a_5\, e_5$ of vector $\boldsymbol{V^a}$, since the value of the corresponding 5th component of vector $\boldsymbol{V^b}$ was zero; similarly, the oligomers in the answer set corresponding to basis vector e_6 would consist solely of the oligomers contributed by component $V^b_6\, e_6$ of vector $\boldsymbol{V^b}$, since the value of the corresponding 6th component of vector $\boldsymbol{V^a}$ was zero;

(c) the oligomers in the answer set corresponding to basis vector e_7 would be represented by the sum of the oligomers representing V^a_7 of $\boldsymbol{V^a}$ and V^b_7 of $\boldsymbol{V^b}$, all of which have the same sequence; and

(d) the concentration of single-stranded oligomers in the answer set corresponding to basis vector $\boldsymbol{e}_8$ would be proportional to the difference in the initial concentrations of the oligomers representing vector components $V^a{}_8\, \boldsymbol{e}_8$ and $V^b{}_8\, \boldsymbol{e}_8$. In this example, only the single-stranded oligomers representing $V^a{}_8\, \boldsymbol{e}_8$ and $V^b{}_8\, \boldsymbol{e}_8$ will hybridize to each other, and the single-stranded oligomers corresponding to basis vector $\boldsymbol{e}_8$ that remain after hybridization of the oligomers representing $V^a{}_8\, \boldsymbol{e}_8$ and $V^b{}_8\, \boldsymbol{e}_8$ will be those which were initially present in the greater concentration.

One skilled in the art would reasonably expect the claimed method to operate successfully in the hypothetical example described above, even though the two vectors $\boldsymbol{V}^a$ and $\boldsymbol{V}^b$ being added together are not oppositely oriented in vector space. The Applicants submit that addition of two or more vectors by the invention described in the specification and recited in claim 13 is accurately represented by the change in relative concentrations of the single-stranded oligomers representing the amplitudes of basis vectors $\boldsymbol{e}_1$ for $i = 1$ to m, as described in the specification, even if none, or only some, of the components of one vector are oppositely oriented in vector space relative to the corresponding components of the other vector. Limiting the claimed method to addition operations in which the vectors are exactly oppositely oriented in space as called for by the rejection stated on page 5 of the Office Action would limit claim 13 to a small subset of vector addition operations consisting of addition of two vectors that are defined by the same set of non-zero basis vectors, where (a) the values of the amplitudes of the components of one vector are of opposite sign to those of the corresponding components of the other vector, and (b) where the absolute values of the amplitudes of the components of one vector are proportional to those of the corresponding components of the other vector. Moreover, if claim 13 was limited as called for in the rejection, it would not be able to encompass addition

of more than two vectors at a time. As discussed above, the specification teaches one skilled in the art how to practice the claimed method to represent addition of any number of m-component vectors which are not oppositely oriented in vector space, without undue experimentation. The Applicants therefore respectfully request that the rejection of claim 13 under 35 U.S.C. 112, 1st paragraph, limiting the claim to a method in which the vectors are oppositely oriented in space, be withdrawn.

B. <u>Regarding the rejection of claims 27 and 28 for unsupported scope</u>:

The Office Action rejects claims 27 and 28 for encompassing a method for inner product determination wherein the vectors are not co-oriented, and states that the claimed methods are only enabled for inner product determination where (i) the vectors are exactly co-oriented in vector space , (ii) the oligomers representing vector components having orthogonal basis vectors do not hybridize, and (iii) the oligomers representing vectors that are partially co-linear hybridize with a degree of intermediate stability that is related to the degree of co-linearity of the vectors.

With regard to the limitation of the claims to methods wherein the vectors are exactly co-oriented in vector space, the Applicants submit that the specification enables one skilled in the art to practice the claimed methods for determining the inner product between two vectors or between a matrix and a vector which are not co-oriented without having to perform undue experimentation. Indeed, in most cases in which the claimed method is practiced, the vectors will probably <u>not</u> be exactly co-oriented.

The specification teaches a method wherein $\boldsymbol{V}$ and $\boldsymbol{W}$ are defined as

$$\boldsymbol{V} = \mathrm{V}_1\, \boldsymbol{e}_1 + \mathrm{V}_2\, \boldsymbol{e}_2 + \mathrm{V}_3\, \boldsymbol{e}_3 + \ldots \mathrm{V}_m\, \boldsymbol{e}_m, \quad \text{and}$$

$$\boldsymbol{W} = \mathrm{W}_1\, \boldsymbol{e}_1 + \mathrm{W}_2\, \boldsymbol{e}_2 + \mathrm{W}_3\, \boldsymbol{e}_3 + \mathrm{W}_m\, \boldsymbol{e}_m,$$

where $\boldsymbol{e}_1$, $\boldsymbol{e}_2$, $\boldsymbol{e}_3$ ... $\boldsymbol{e}_m$, are basis vectors in m-space that are each represented by a pair of complementary oligomers E_i and $\underline{E}_i$, the concentrations of which are proportional to the absolute values of the positive and negative values, respectively, of the corresponding amplitudes of the vector components (see page 5, lines 2-15). In order for vectors $\boldsymbol{V}$ and $\boldsymbol{W}$ to be exactly co-oriented, the values of the components $V_1, V_2, V_3, \ldots V_m$ of $\boldsymbol{V}$ would all have to have the same sign and be exactly proportional to the corresponding components $W_1, W_2, W_3, \ldots W_m$ of $\boldsymbol{W}$. However, the methods described in the specification permit one to represent the determination of the inner product of two vectors, or of a vector and a matrix, even when the values and signs of the components are randomly assigned.

For example, the inner product of $\boldsymbol{V}$ and $\boldsymbol{W}$ is:

$$\boldsymbol{V} \cdot \boldsymbol{W} = V_1W_1 + V_2W_2 + V_3W_3 + \ldots V_mW_m$$

(see Riddle, Calculus and Analytic Geometry, 2nd Edition, Wadsworth Publishing Co., Belmont, Ca, 1974, pages 620-621). As described in the specification, the hybridization rates R_- and R_+ of corresponding vector components are proportional to the terms V_1W_1 to V_mW_m which make up the inner product (see pages 31-33), since vector amplitudes V_i and W_i for i = 1 to m are proportional to the concentrations of the oligomers that represent the corresponding basis vectors $\boldsymbol{e}_i$ for i = 1 to m, and the rate of hybridization of complementary oligomers is proportional to the product of their concentrations. In the case where a vector component is zero, the contribution to the inner product for that component will also be zero, since there are no oligomers in the reaction mixture corresponding to the component of zero amplitude. One skilled in the art would recognize that this correlation between the rate of hybridization of oligomers representing the components of the vectors and the inner product of the vectors holds whether or not the vectors are co-oriented.

With regard to the limitation that the claims be restricted to methods wherein the oligomers representing vector components having orthogonal basis vectors do not hybridize, the Applicants note that oligomers of different basis vectors do not hybridize, even when they are not orthogonal, and that claims 27 and 28 are amended to recite that the oligomers that represent components of the recited vectors and/or matrix having different basis vectors do not hybridize under conditions in which complementary oligomers E_i and $\underline{E_i}$ corresponding to the same basis vector $\boldsymbol{e}_i$ do hybridize, as described in the specification at pages 27, lines 5-14, and page 28, lines 10-12.

With regard to the limitation that the claims be restricted to methods in which oligomers representing vectors that are partially co-linear are able to partially hybridize to each other, the Applicants submit that the present invention does not call for the use of oligomers that only partially hybridize; according to the present invention, vectors that are at least partially co-linear have at least one component that is non-zero for the same basis vector $\boldsymbol{e}_i$, and oligomers that represent the components of different basis vectors do not hybridize under conditions in which complementary oligomers E_i and $\underline{E_i}$ that represent positive and negative values of the same basis vector $\boldsymbol{e}_i$ do hybridize, as described in the specification and as discussed above.

In view of the above, the Applicants submit that the specification teaches one skilled in the art how to practice the methods of claims 27 and 28 without undue experimentation, whether or not the vectors are exactly co-oriented, and without requiring the use of oligomers that partially hybridize to represent partially co-linear vectors, and therefore respectfully request that the rejection of claims 27 and 28 under 35 U.S.C. 112, 1st paragraph, limiting the claims to be withdrawn.

C. Regarding the rejection of claim 15 for unsupported scope:

The Office Action rejects claim 15 because the claim does not recite a method step disclosed in the specification by which the recited set of single-stranded oligomers representing the outer product matrix of vectors ***V*** and ***W*** is prepared or obtained, so as to enable one to make or use the invention. The Applicants submit that the specification teaches at least two different methods by which one skilled in the art could obtain the recited set of oligomers representing the outer product matrix of two vectors, and that a skilled artisan would have known of other, routine methods by which this could be done, so that the specification enables one skilled in the art to practice the claimed method for without having to perform undue experimentation.

The specification teaches that an outer product matrix of two vectors can be formed by joining the 3' ends of the single-stranded DNA oligomers corresponding to one of the vectors to the 5' termini of the DNA oligomers corresponding to the other vector (page 33, lines 20-22). One skilled in the art would recognize that for vectors ***V*** and ***W*** defined as:

$$\boldsymbol{V} = V_1 \boldsymbol{e}_1 + V_2 \boldsymbol{e}_2 + V_3 \boldsymbol{e}_3, \quad \text{and}$$

$$\boldsymbol{W} = W_1 \boldsymbol{e}_1 + W_2 \boldsymbol{e}_2 + W_3 \boldsymbol{e}_3,$$

the outer product matrix ***T*** would be:

$$\begin{matrix} V_1W_1 & V_1W_2 & V_1W_3 \\ V_2W_1 & V_2W_2 & V_2W_3 \\ V_3W_1 & V_3W_2 & V_3W_3 \end{matrix}$$

A method for preparing a set of oligomers representing the outer product matrix of two vectors V_i and W_j is described on pages 33-34 of the specification, which teaches that an outer product matrix of two vectors can be formed by removing the 5' phosphates from a set of oligomers representing one vector, and ligating these oligomers to a set of oligomers having

phosphorylated 5' termini that represent the other vector. The specification also teaches that oligomers of the present invention can be synthesized by routine methods of oligonucleotide synthesis (page 14, lines 22-25). Such methods include either chemical synthesis or template-mediated synthesis employing a commercially available DNA polymerase. Applicants therefore submit that at the time of filing, a skilled artisan would have been able to follow any of several methods described in the specification or known in the art to practice the claimed method, and respectfully request that the rejection of claim 15 under 35 U.S.C. 112, 1st paragraph, limiting the claims to methods in which a specific method for obtaining oligomers corresponding to an outer product matrix is specified, be withdrawn.

<u>Rejection of claims 22-24 under 35 U.S.C. 112, 2nd paragraph, as being indefinite</u>

The Office Action rejects claims 22-24 as being indefinite because the antecedent basis in claim 17 for "said single-stranded oligomers" recited in claim 22 is unclear, and because the precise meaning of terms "complete" and "sub-stoichiometric" is also unclear.

With regard to the antecedent basis in claim 17 for "said single-stranded oligomers," claim 22 is amended to identify the recited oligomers as those recited in step (c) of claim 17.

With regard to the meaning of "complete" and "sub-stoichiometric" recited in step (c) of claim 17 and in claim 22, step (c) of claim 17 has also been amended to state that the recited set of E_i and $\underline{E}_i$ oligomers represent "the complete set of basis vectors $\boldsymbol{e}_i$ for i = 1 to m, wherein the E_i and $\underline{E}_i$ oligomers are sub-stoichiometric relative to said set of X_i oligomers, in that the number of X_i oligomers for at least one basis vector $\boldsymbol{e}_i$ is greater than the number of E_i or $\underline{E}_i$ saturating oligomers corresponding to said basis vector." Applicants submit that one skilled in the chemical arts would understand that the term "stoichiometric" refers to the relationship between

phosphorylated 5' termini that represent the other vector. The specification also teaches that oligomers of the present invention can be synthesized by routine methods of oligonucleotide synthesis (page 14, lines 22-25). Such methods include either chemical synthesis or template-mediated synthesis employing a commercially available DNA polymerase. Applicants therefore submit that at the time of filing, a skilled artisan would have been able to follow any of several methods described in the specification or known in the art to practice the claimed method, and respectfully request that the rejection of claim 15 under 35 U.S.C. 112, 1st paragraph, limiting the claims to methods in which a specific method for obtaining oligomers corresponding to an outer product matrix is specified, be withdrawn.

Rejection of claims 22-24 under 35 U.S.C. 112, 2nd paragraph, as being indefinite

The Office Action rejects claims 22-24 as being indefinite because the antecedent basis in claim 17 for "said single-stranded oligomers" recited in claim 22 is unclear, and because the precise meaning of terms "complete" and "sub-stoichiometric" is also unclear.

With regard to the antecedent basis in claim 17 for "said single-stranded oligomers," claim 22 is amended to identify the recited oligomers as those recited in step (c) of claim 17.

With regard to the meaning of "complete" and "sub-stoichiometric" recited in step (c) of claim 17 and in claim 22, step (c) of claim 17 has also been amended to state that the recited set of E_i and $\underline{E_i}$ oligomers represent "the complete set of basis vectors $\boldsymbol{e}_i$ for i = 1 to m, wherein the E_i and $\underline{E_i}$ oligomers are sub-stoichiometric relative to said set of X_i oligomers, in that the number of X_i oligomers for at least one basis vector $\boldsymbol{e}_i$ is greater than the number of E_i or $\underline{E_i}$ saturating oligomers corresponding to said basis vector." Applicants submit that one skilled in the chemical arts would understand that the term "stoichiometric" refers to the relationship between measured quantities of substances or energies involved in a chemical reaction (see J. Bailar, "Stoichiometry," in McGraw-Hill Encyclopedia of Science and Technology, 6th Edition,

McGraw-Hill Book co., New York, 1987, Vol. 17, pp. 436-437, copy attached). Accordingly, Applicants submit that the meaning of claims 22-24, as amended, would be clearly understood by one skilled in the art, and respectfully request that the rejection of claims 22-24 under 35 U.S.C. 112, 2nd paragraph, be withdrawn.

Rejection of claims 9-11 under 35 U.S.C. 102(b) as being anticipated by the prior art

The Office Action rejects claims 9-11 as being anticipated by either Adleman, Guarnieri et al., or Oliver.

Applicants submit that the present invention is qualitatively different and patentably distinct from the cited prior art methods. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. 7th Edition, § 2131, citing Verdegal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); and "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." M.P.E.P. 7th Edition, § 2131, citing Richardson v. Suzuki Motor Co., 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Adleman describes a method for solving a directed Hamiltonian path problem which does not employ oligomers representing both positive and negative values, and the abstracts of both the Guarnieri et al. and Oliver et al. references explicitly state that the analog methods described by these references only permit addition and matrix multiplication of non-negative numbers.

Claims 9-11 explicitly recite a method wherein oligomers are used to represent vector or matrix components having either positive or negative sign (see claim 9, lines 7-9); and the specification clearly states that this feature of the claimed invention is a significant advance over the prior art (see page 3, lines 1-5). Applicants submit that none of the cited prior art references discloses, explicitly or inherently, a method for determining a mathematical result of carrying out an operation of matrix algebra in which both positive and negative vector components are represented by oligomers as recited in claims 9-11.

Moreover, step (3) of claim 9 is amended to recite that the "analog result of carrying out said operation of matrix algebra on said input data is quantitatively dependent on the concentrations of said at least one set of single-stranded oligomers E_i and E_i in said composition." In each of the examples of the claimed invention disclosed in the specification, the mathematical result of carrying out an operation of matrix algebra that is obtained by the claimed method depends quantitatively on the concentrations of the input oligomers. In contrast, the results obtained by the cited prior art methods depend on sequence-specific hybridization reactions of oligomers, but are not quantitatively dependent not on the respective concentrations of the oligomers.

In view of the above, Applicants submit that claims 9-11 are not anticipated by the cited prior art references under 35 U.S.C. § 102(b), and respectfully request withdrawal of the rejection.

The Examiner is invited to contact the undersigned Applicant's representative if he thinks that an interview would be helpful in clarifying any issues associated with the prosecution of this application.

Respectfully submitted,

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